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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/601,171	06/23/2003	Gerald W. Fischer	103901-4197	4940

959 7590 04/17/2009

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EXAMINER	
ARCHIE, NINA	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
04/17/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/601,171	FISCHER ET AL.	
	Examiner	Art Unit	
	Nina A. Archie	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/3/2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *61-63,65-68,77,79-81,86,87,91,93-101 and 104-115* is/are pending in the application.

4a) Of the above claim(s) *96-100* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *61-63, 65-68, 77, 79-81, 86-87, 91, 93-95, 101, and 104-115* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/3/2008 and 09/09/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office is responsive to Applicant's amendment and response filed 9-9-08 and 12-3-08. Claims 61-63, 65-68, 77, 79-81, 86-87, 91, 93-101, and 104-115 are pending. Claims 61-63, 65-68, 77, 79-81, 86-87, 91, 93-95, 101, and 104-115 are under examination. Claims 61, 77, 87, 95, and 101 have been amended. Claims 96-100, has been withdrawn.

Rejections Withdrawn

2. In view of the Applicant's amendment and remark following rejections are withdrawn.

a) The rejection of claim 61under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the phrase "binding affinity of about" is withdrawn in light of amendment thereto.

b) The rejection of claim 86 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by being dependent on a canceled claim is withdrawn in light of applicant's amendment thereto.

c) The rejection of claims 61-63, 65-68, 77, 79-81, 86-87, 91, 93-95, 101, and 104-115 under 35 U.S.C. 112, first paragraph, the new matter based on the limitation "binding affinity of about 10^{-8} M" is withdrawn in light of applicant's cancellation of claims.

d) The rejection of claims 61-62 and 65-67, 81, 86-87, and 93 are rejected under 35 U.S.C. 102(b) as being anticipated by Hamada et al 1984, Microbiol. Immunol. Vol. 28 No. 9 pgs. 1009-1021 in light of Roitt et al, 1993, Immunology, 3rd Edition, Mosby, St is withdrawn in light of applicant's argument and the limitation of enhancing opsonization is not disclosed by the art.

c) The rejection of claims 107-109 and 111-115 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in lieu of the rejection set forth below.

Claim Objections Maintained

3. The objection to claim 67 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is maintained for reasons of record. It should be noted that Applicant did not address this objection in his response.

As outlined previously, claim 67 is drawn to a monoclonal antibody of claim 61, wherein the antibody is capable of binding to LTA of Gram positive bacteria fixed to a solid support does not further limit the structure of the monoclonal antibody in claim 61. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim Rejections Maintained

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. The rejection of claims 61, 77, 79, 93 and 95 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7, 9-12,14-19 of U.S. Patent No. 6,610,293 are maintained for the reason set forth in the previous office action.

Applicants states in Applicants Arguments/Remarks on 9/9/08, will consider filing a terminal disclaimer over the 6,610,293.

5. The rejection to claims 77, 81, 86-87, 93 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 53-58, 79-83 of copending Application No. 11/193,440 are maintained for the reason set forth in the previous office action.

Applicants states in Applicants Arguments/Remarks on 9/9/08, will address any obviousness-type double patenting issues upon an indication of allowance claims in Application NO. 11/193,440.

6. The claims 77, 79-81, 86-87, and 93 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 40-43 and 47-68 and 72 of copending Application No. 10/323,926 are maintained for the reason set forth in the previous office action.

Applicants states in Applicants Arguments/Remarks on 9/9/08, will address any obviousness-type double patenting issues upon an indication of allowance claims in Application NO. 11/323,926.

7. The claims 61,101 and 104-115 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6, 9-12,14-19 of U.S. Patent No. 6,610,293 are maintained for the reasons set forth in the previous office action.

Applicants states in Applicants Arguments/Remarks on 9/9/08, will consider filing a terminal disclaimer over the 6,610,293.

8. The claims 104-115 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 53, 83, 91-92, and 96 of copending Application No. 11/193,440 are maintained for the reasons set forth in the previous office action.

Applicants states in Applicants Arguments/Remarks on 9/9/08, will address any obviousness-type double patenting issues upon an indication of allowance claims in Application NO. 11/193,440.

New Grounds of Rejections

35 USC § 112

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 61, 62-63, 65-68, 79-81, 86-87, 91, 94, 101, and 114-115 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is written description rejection.

Applicant is directed to the Guidelines for the Examination of Patent Applications under the 35 U.S.C. 112, first paragraph "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The instant claims are drawn to a composition comprising an amount of a monoclonal antibody effective to prevent staphylococcal infection in neonates and a pharmaceutically acceptable carrier, wherein the antibody specifically binds to poly-glycerol phosphate of Lipoteichoic acid (LTA) of Gram positive bacteria and is of the IgG isotype, wherein the antibody binds to and enhances opsonization of multiple serotypes of *Staphylococcus epidermidis*, coagulase negative staphylococci, *Staphylococcus aureus*, and *Streptococcus mutans* by phagocytic cells with or without complement as compared to an appropriate control in an in vitro opsonization assay.

To fulfill the written description requirements set forth under 35 USC § 112, first paragraph, the specification must describe at least a substantial number of the members of the claimed genus, or alternatively describe a representative member of the claimed genus, which shares a particularly defining feature common to at least a substantial number of the members of the claimed genus, which would enable the skilled artisan to immediately recognize and distinguish its members from others, so as to reasonably convey to the skilled artisan that Applicant has possession the claimed invention. To adequately describe the genus of a composition comprising a monoclonal antibody with the recited characteristics, applicant must adequately describe the antigenic determinants (immunoepitopes) based on the ability to a) prevent any and all staphylococcal infections in neonates, b) bind to poly-glycerol phosphate of LTA, and c) enhance opsonization of *Staphylococcus epidermidis*, coagulase negative staphylococci, *Staphylococcus aureus*, and *Streptococcus mutans*.

The specification discloses the chimeric monoclonal antibody/monoclonal antibody 96-110 bound to both coagulase positive and negative and enhanced opsonization (see pgs. 45-46 Examples 2). The specification discloses anti-LTA MAB for *Staphylococci* epidermidis and demonstrates enhanced opsonic activity (see pgs. 66-67 Example 11). The specification discloses in vivo efficacy administering chimeric monoclonal antibody (chimeric MAB) /monoclonal 96-110 (MAB 96-110) which shows survival of mice but not prevention of any staphylococcal infection (Examples 3 and 12-13 pgs. 67-71). The specification discloses MAB 96-110 against Lipotechoic Acid from

bacteria such as *Streptococcus mutans, Staphylococcus aureus, Streptococcus faecalis, and Streptococcus pyogenes* (Example 7 Table 8 pg. 52-55). These disclosures do not provide adequate description of the claimed genus of antibodies.

Applicant has not demonstrated that a composition comprising any monoclonal antibody that possess the abilities of the claimed monoclonal antibodies. The limited number of composition comprising a monoclonal antibody of IgG isotype disclosed is not deemed to be representative of the genus encompassed by the instant claims. The specification, does not disclose distinguishing and identifying features of a representative number of members of the genus of a composition comprising a monoclonal antibody of the IgG isotype, to which the claims are drawn, such as a correlation between the structure of the immunoepitope and its recited function (a) prevent staphylococcal infections in neonates, b) wherein said antibody binds to poly-glycerol phosphate of LTA, and c) and which enhances opsonization of the *Staphylococcus epidermidis*, coagulase negative staphylococci, *Staphylococcus aureus*, and *Streptococcus mutans*), so that the skilled artisan could immediately envision, or recognize at least a substantial number of members of the claimed genus of a composition comprising a monoclonal antibody of the IgG isotype.

Moreover the specification fails to disclose the protective immunoepitope(s) of a composition comprising a monoclonal antibody. Therefore, since the specification fails to adequately describe at least a substantial number of members of the genus of the monoclonal antibody aforementioned above to which the claims are based; the specification fails to adequately describe at least a substantial number of members of the claimed genus of a composition comprising a monoclonal antibody of the IgG isotype possessing the recited functions.

Moreover a vaccine is defined as "a prophylactic or therapeutic material containing antigens derived from one or more pathogenic organisms which, on administration to man or animal, will stimulate active immunity and protect against infection with these or related organism (i.e. produce protective immunity)." (The Dictionary of Immunology, Herbert et al eds, Academic Press, 1995).

MPEP § 2163.02 states, "[a]n objective standard for determining compliance with

the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed' ". The courts have decided:

The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*.

See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.,* 18 USPQ2d 1016.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description" Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). Moreover, because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant were in possession of the claimed invention at the time the application was filed.

The *Guidelines* further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species *cannot* be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. As evidenced by Greenspan et al. (*Nature Biotechnology* 7: 936-937, 1999), defining epitopes is not as easy as it seems. Greenspan et al. recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody is necessary to define an "epitope" (page 937, column 2). According to Greenspan et al., an epitope will include residues that make contacts with a ligand, here the antibody, but are energetically neutral, or even destabilizing to binding. Furthermore, an epitope will not include any residue not contacted by the antibody, even though substitution of such a residue might profoundly affect binding. Accordingly, it follows that the immunoepitopes that can elicit a protective immune response to a given pathogen can only be identified empirically. Therefore, absent a detailed and particular description of a representative number, or at least a substantial number of the members of the genus of immunoepitopes, the skilled artisan could not immediately recognize or distinguish members of the claimed genus of a composition comprising a monoclonal antibody with the recited activities. Therefore, because the art is unpredictable, in accordance with the *Guidelines*, the description of immunoepitopes (antigenic determinants) is not deemed representative of the genus of a composition comprising a monoclonal antibody to which the claims refer and therefore the claimed invention is not properly disclosed.

11. Claims 77, 79-81, 86-87, 91, 93-95, and 104-113 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is written description rejection.

Applicant is directed to the Guidelines for the Examination of Patent Applications under the 35 U.S.C. 112, first paragraph "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The independent claim 77 and all dependent claims 77, 79-81, 86-87, 91, and 93-95, is drawn to a composition comprising a monoclonal antibody, which specifically binds to a polyglycerol phosphate of LTA of Gram positive bacteria, or antigen binding fragment thereof, and a pharmaceutically acceptable carrier, wherein the monoclonal antibody comprises the complementarity determining regions (CDRs) of the heavy and light chain variable regions of monoclonal antibody 96-110 as set forth as SEQ ID NO: 87 and SEQ ID NO: 89.

The independent claims 104-105 are drawn to a composition comprising a monoclonal antibody, which specifically binds to a polyglycerol phosphate of LTA of Gram positive bacteria, or antigen binding fragment thereof, and a pharmaceutically acceptable carrier, wherein the monoclonal antibody of the heavy chain (claim 104) and light chain (claim 105) variable regions of monoclonal antibody as set forth as SEQ ID NO: 87 (claim 104) and SEQ ID NO: 89 (claim 105).

The independent claims 106 and 110 and all dependent claims 107-109 and 111-113 are drawn to a composition comprising a monoclonal antibody, wherein the monoclonal antibody comprises a heavy chain comprising the heavy chain complementarity determining regions (CDRs) of the monoclonal antibody 96-110 and variable region having 80% (claim 106) , 85% (claim 107), 90% (claim 108), and 95% (claim 109) amino acid identity with SEQ ID NO: 87; and light chain comprising the light chain complementarity determining regions (CDRs) of the monoclonal antibody 96-110 and variable region having 80% (claim 110), 85% (claim 111), 90% (claim 112), and 95% (claim 113) amino acid identity with amino acid identity with SEQ ID NO: 89.

To fulfill the written description requirements set forth under 35 USC § 112, first paragraph, the specification must describe at least a substantial number of the members of

the claimed genus, or alternatively describe a representative member of the claimed genus, which shares a particularly defining feature common to at least a substantial number of the members of the claimed genus, which would enable the skilled artisan to immediately recognize and distinguish its members from others, so as to reasonably convey to the skilled artisan that Applicant has possession the claimed invention.

To adequately describe the genus of compositions comprising a monoclonal antibody with the recited characteristics, applicant must adequately describe the antigenic determinants (immunoepitopes) that convey the ability to bind to poly-glycerol phosphate of LTA of a Gram positive organism not just those determinants that would bind to poly-glycerol phosphate of LTA itself.

The specification discloses the chimeric monoclonal antibody/monoclonal antibody 96-110 bound to both coagulase positive and negative and enhanced opsonization (see pgs. 45-46 Examples 2). The specification discloses anti-LTA MAB for *Staphylococci* epidermidis and demonstrates enhanced opsonic activity (see pgs. 66-67 Example 11). The specification discloses MAB 96-110 against Lipotechoic Acid from bacteria such as *Streptococcus mutans, Staphylococcus aureus, Streptococcus faecalis, and Streptococcus pyogenes* (Example 7 Table 8 pg. 52-55).

The data indicated above does not correlate to the claimed functions set forth in the instant claims. Applicant has not demonstrated that a composition comprising variants of monoclonal antibody of IgG isotype aforementioned above is capable binding to poly-glycerol phosphate of LTA of all gram positive bacteria species discussed above.

The specification, however, does not disclose distinguishing and identifying features of a representative number of members of the genus aforementioned above to which the claims are drawn, such as a correlation between the structure of the immunoepitope and its recited function (binding to poly-glycerol phosphate of LTA), so that the skilled artisan could immediately envision, or recognize at least a substantial number of members of the claimed genus of compositions aforementioned above. Moreover, the specification fails to disclose which amino acid residues are essential to the function of the immunoepitope or which amino acids might be replaced so that the resultant immunoepitope retains the activity of its parent, or by which other amino acids

the essential amino acids might be replaced so that the resultant immunoepitope retains the activity of its parent. Also the specification fails to disclose which variable regions of the heavy and light chain of a monoclonal antibody of SEQ ID NO: 87 and 89; and of the monoclonal antibody 96-110 that are essential to the function of the immunoepitope and are able to retains its the activity. Therefore, since the specification fails to adequately describe at least a substantial number of members of the genus of the compositions comprising a monoclonal antibody aforementioned above to which the claims are based capable binding specifically to poly-glycerol phosphate of LTA.

MPEP § 2163.02 states, "[a]n objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed' ". The courts have decided:

The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed.*

See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.,* 18 USPQ2d 1016.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description" Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). Moreover, because the claims encompass a genus of variant species, an adequate written description

of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant were in possession of the claimed invention at the time the application was filed.

The *Guidelines* further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species *cannot* be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. As evidenced by Greenspan et al. (*Nature Biotechnology* **7**: 936-937, 1999), defining epitopes is not as easy as it seems. Greenspan et al. recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody is necessary to define an "epitope" (page 937, column 2). According to Greenspan et al., an epitope will include residues that make contacts with a ligand, here the antibody, but are energetically neutral, or even destabilizing to binding. Furthermore, an epitope will not include any residue not contacted by the antibody, even though substitution of such a residue might profoundly affect binding. Accordingly, it follows that the immunoepitopes that can elicit a protective immune response to a given pathogen can only be identified empirically. Furthermore the specification lacks written description of the instant variants that specifically bind to polyglycerol phosphate of LTA. For example, Colman et al. (Research in Immunology 145: 33-36, 1994, p.33 column 2, p. 35 column 1) disclose that a single amino acid changes in an antigen can effectively abolish the interaction with an antibody entirely and that a very conservative amino acid substitution may abolish antibody binding and a non-conservative amino substitution may have little effect in antibody binding. This underlies the importance of the description of the

immunoepitopes that are protective and which conservative amino acid substitutions and where and how many changes can the immunoepitopes tolerate and still retain the ability to protect from infection. Therefore, absent a detailed and particular description of a representative number, or at least a substantial number of the members of the genus of compositions comprising a monoclonal antibody with the claimed characteristics, the skilled artisan could not immediately recognize or distinguish members of the claimed genus of compositions aforementioned above capable of binding specifically to poly-glycerol phosphate of LTA on Gram positive bacteria. Therefore, because the art is unpredictable, in accordance with the *Guidelines*, the description of immunoepitopes (antigenic determinants) is not deemed representative of the genus of compositions comprising a monoclonal antibody aforementioned above, to which the claims refer and therefore the claimed invention is not properly disclosed.

Enablement

12. Claims 61-63, 65-68, 79-81, 86-87, 91, 94, and 101, and 114-115 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contain subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is not enabled for a composition comprising an amount of an isolated a monoclonal antibody effective to prevent staphylococcal infection in neonates and a pharmaceutically acceptable carrier,

Furthermore, the specification does not reasonably enable any composition comprising an amount of an isolated a monoclonal antibody effective to prevent staphylococcal infection in neonates and a pharmaceutically acceptable carrier. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claimed invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01 (A)). These include: nature of the invention, breadth of the claims, guidance of the

specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary.

(A) The nature of the invention;

(B) The breadth of the claims;

(C) The state of the prior art;

(D) The level of one of ordinary skill;

(E) The level of predictability in the art;

(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Nature of the invention: The instant claims are drawn to any composition: comprising an amount of an isolated a monoclonal antibody of IgG isotype effective to prevent staphylococcal infection in neonates and a pharmaceutically acceptable carrier.

Breadth of the claims: The claims encompass any composition: comprising an amount of an isolated a monoclonal antibody which specifically binds to poly- glycerol phosphate of Lipoteichoic acid (LTA) of Gram positive bacteria and is of the IgG isotype, binds to and enhances opsonization of multiple serotypes of *Staphylococcus epidermidis*, coagulase negative staphylococci, *Staphylococcus aureus*, and *Streptococcus mutans* by phagocytic cells with or without complement as compared to an appropriate control in an in vitro opsonization assay and is effective to prevent any type of staphylococcal infection in neonates (which encompasses infections of the skin such as impetigo (a crusting of the skin) or cellulitis (inflammation of the connective tissue under the skin, leading to swelling and redness of the area) and staphylococcal sepsis (infection in the bloodstream).

Guidance of the specification/The existence of working examples:

The specification discloses in vivo efficacy administering chimeric monoclonal antibody (chimeric MAB) /monoclonal 96-110 (MAB 96-110) which shows survival of mice but not prevention (Examples 3 and 12-13 pgs. 67-71). There was no prevention

against any type of *Staphylococcus* species offered by chimeric monoclonal antibody/monoclonal antibody 96-110, indicating that immunization with chimeric monoclonal antibody/monoclonal antibody 96-110 alone is insufficient to elicit protection in contrast to the claimed invention. The specification discloses chimeric monoclonal antibody/monoclonal antibody 96-110 promote clearance of the staphylococci from the blood (see pg. 71) .

However, the specification is only limited to the survival of neonates through the administration of the MAB 96-110. The claimed invention is drawn to prevention of staphylococcal infection and as result prevention is correlated to a vaccine. A vaccine by definition must provide protection against an infection demonstrable by challenge experiments. The data as set forth supra does not demonstrate that the composition confers "protection" against infection by *Staphylococcus.* The data merely shows that said composition increases the number of neonates that survived from *Staphylococcus* infection. Therefore the data fails to show prevention or vaccine protection against *Staphylococcus* species. Therefore, one skilled in the art would not accept on its face the examples given in the specification as being correlative or representative of a successful model. The working examples do not disclose any empirical data or results indicative of a preventing *Staphylococcus* infection as claimed. The specification is devoid of any teaching that the claimed prevents staphylococcal infection in neonates.

State of the art: Although many investigators have tried to develop vaccines based on specific antigens, it is well understood that the ability of an antigen to stimulate antibody production does not necessarily correlate with the ability of the antigen to stimulate an immune response capable of protecting an animal from infection (Chandrasekhar et al., US Patent 6,248,329, col. 1, lines 35-41). It is well recognized in the vaccine art, that it is unclear whether an antigen derived from a pathogen will elicit protective immunity. Ellis (Chapter 29 of Vaccines, Plotkin, et al. (eds) WB Saunders, Philadelphia, 1998, especially p. 571, paragraph 2) exemplifies this problem in the recitation that "the key to the problem (of vaccine development) is the identification of that protein component of a virus or microbial pathogen that itself can elicit the

production of protective antibodies.., and thus protect the host against attack by the pathogen." As evidenced by Greenspan et al. (*Nature Biotechnology* 7: 936-937, 1999), defining epitopes is not as easy as it seems. Greenspan et al. recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody is necessary to define an "epitope" (page 937, column 2). According to Greenspan et al., an epitope will include residues that make contacts with a ligand, here the antibody, but are energetically neutral, or even destabilizing to binding. Furthermore, an epitope will not include any residue not contacted by the antibody, even though substitution of such a residue might profoundly affect binding. Accordingly, it follows that the immunoepitopes that can elicit a protective immune response to a given pathogen can only be identified empirically. For the reasons set forth supra, the state of the art is has limitations to a composition comprising a monoclonal antibody aforementioned above and the state of the art is unpredictable with regard any composition as set forth supra comprising a monoclonal antibody.

In conclusion, the claimed invention is not enabled for any composition comprising an amount of an isolated a monoclonal antibody effective to prevent staphylococcal infection in neonates and a pharmaceutically acceptable carrier. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claimed invention. The claims encompass any composition: comprising an amount of an isolated a monoclonal antibody of IgG isotype effective to prevent any type of staphylococcal infection in neonates which encompasses infections of the skin such as impetigo (a crusting of the skin) or cellulitis (inflammation of the connective tissue under the skin, leading to swelling and redness of the area) and staphylococcal sepsis (infection in the bloodstream). The specification fails to teach that the composition as set forth can produce a protective response in the host, for prevention of staphylococcal in neonates, as is requisite of a vaccine composition. The state of the art teaches that there are limitations to a vaccine composition and the state of the art is unpredictable. In view of the lack of support in the art and specification for an effective vaccine, it would require undue

experimentation on the part of the skilled artisan to make and use the vaccine as claimed; therefore the claims are not enabled. As a result, for the reasons discussed above, it would require undue experimentation for one skilled in the art to use the claimed composition.

Conclusion

13. No claims allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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